IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW YORK

BARBARA SCHWAB, *et al.*,

Plaintiffs,

v.

PHILIP MORRIS USA, INC., *et al.*,

Defendants.

Civil Action No. CV 04-1945 (JBW)

DECLARATION OF JANE Y. LEWIS, PH.D.

I. Background of Declarant

1. I am employed by Philip Morris USA Inc. (hereinafter "Philip Morris USA"), and my current position is Vice President of Product Assessment in the Research, Development and Engineering Department. I have been employed by Philip Morris USA since 1984 and since that time I have worked in various departments, including the Analytical Research Division, the Product Testing Laboratory, the New Technology Research Division, and the Quality Assurance Department.

2. As the Vice President of Product Assessment in the Research, Development and Engineering Department at Philip Morris USA, my responsibilities include supervision of chemical, biological and clinical testing of research and prototype cigarettes, as well as quality assurance and compliance with U.S. and state cigarette testing and reporting requirements. In addition, I am specifically responsible for managing the team at Philip Morris USA that supervises the Total Exposure Study ("TES") and that is responsible for overseeing the analysis of the data collected, ensuring accuracy of the data, and organizing and presenting the data to the public.

II. The Total Exposure Study (TES)

A. Background and Purpose of the TES

3. The TES is a massive ongoing research study designed and sponsored by Philip Morris USA. Philip Morris USA scientists engaged in constructive dialogue with members of the scientific and public health communities, including Dr. David Burns of the University of California-San Diego, and Dr. Greg Connolly (former Director of the Tobacco Control Program of the Massachusetts Department of Public Health) on the design, protocols, and methods used to conduct the TES, as well as a Pilot TES Study and a follow-up study to the TES. Philip Morris USA modified the TES design based on these dialogues.

4. The TES is a cross-sectional, observational study of close to 5000 adult participants (3585 smokers and 1077 nonsmokers) at 39 locations across the U.S. Its primary objectives are (a) to estimate the exposure of adult U.S. cigarette smokers to cigarette smoke constituents using selected biomarkers of exposure and biologically effective dose; and (b) to investigate the relationship between cigarette smoke exposure of U.S. adult smokers and tar delivery across all tar yield categories as measured by the FTC method. In layman's terms, the TES uses different types of experimental measures to investigate the total amount of smoke (e.g., nicotine, tar, and other smoke constituents) to which different people are exposed from smoking cigarettes with different tar and nicotine yields as measured by the FTC method.

5. The fact that the TES employs a "cross-sectional, observational" design means that data from each individual study participant were collected at a single point in time. The TES did not involve switching between brands, but instead collected data

based on individual participants smoking their usual brand of cigarettes at a single point in time. The term "compensation" is used herein to describe a series of potential changes in smoking behavior that may result when an individual switches from one cigarette brand to a brand with a different FTC tar and nicotine yield. For example, a smoker who switches to a cigarette with a lower tar yield may compensate by smoking more cigarettes or by smoking individual cigarettes with greater intensity (bigger puffs, more frequent puffs, etc.). The design of the TES means that the TES cannot resolve fully questions relating to whether (or to what extent) individual smokers engage in compensation.

6. The TES was not conceived, designed, or executed for litigation. The TES serves an important business and public health function – specifically, to support the development of potential reduced exposure or risk products, also known as "PREPs." Reducing the harm caused by smoking is a priority of Philip Morris USA. Towards that goal, Philip Morris USA is striving to develop new and innovative products that reduce the levels of toxic and carcinogenic substances that are delivered to smokers. Members of the public health community have stated that they consider it important to compare these potential new products with cigarettes currently on the market based on smokers' exposure to specific smoke constituents as measured by "biomarkers of exposure" or other methods.

7. A "biomarker" is a smoke constituent or metabolite of a smoke constituent that can be measured in body fluids such as urine or blood. Biomarkers are frequently used to estimate an individual's exposure to specific smoke constituents. For example, nicotine is sometimes used as a biomarker, as are a number of its metabolites, such as cotinine and *trans*-3'-hydroxycotinine. The TES, like a number of published scientific

studies of smoking exposure, uses biomarkers as a measure of exposure to various smoke constituents. The TES collected data for fifteen biomarkers of exposure, including nicotine and its metabolites, COHb (biomarker for carbon monoxide), 1-OHP (biomarker for PAH), and NNAL (biomarker for TSNA). The TES also collected data for nineteen biomarkers of potential harm, which are measurements of an effect due to exposure, such as inflammation, lipid levels, blood clotting, etc.

8. Biomarker data must be interpreted with caution – particularly when used to compare different smokers – due to substantial inter-individual variability in the absorption, distribution, metabolism, and elimination of smoke constituents. These sources of variability are not taken into account by mere statistical and computational analysis of biomarker data.

9. The TES also collected demographic and survey data, as well as smoking topography. Studies of smoking topography collect data on how people puff cigarettes (e.g., number of puffs, puff volume, puff duration).

10. Prior to conducting the TES, Philip Morris USA designed and conducted a Pilot Study. The purpose of the Pilot Study was to test and validate the design concepts for the subsequent larger study (TES), to determine the level of variation in actual human measures, and to determine the level of sensitivity of the bioanalytical methods. The final report of the Pilot Study was completed in the first quarter of 2004, and Philip Morris USA scientists have submitted a manuscript of their findings for publication in a peer-reviewed journal. The Pilot Study resulted in at least eight formal poster presentations at open scientific conferences, including meetings of the Society for Research on Nicotine and Tobacco, the Society of Toxicology, and the American

Association for Cancer Research. Philip Morris USA scientists have also given presentations about the TES to the U.S. Centers for Disease Control and Prevention, the Institute of Medicine of the National Academies of Sciences, State Attorneys General, the Massachusetts Department of Public Health, and the World Health Organization.

11. In addition, Philip Morris USA has designed and executed a follow-up study to the TES. The follow-up study, which was suggested by Dr. David Burns, identified smokers who since participating in the TES had spontaneously switched to a cigarette with an FTC tar yield at least 3 mg higher or lower than the brand they were smoking at the time of the TES. Biological samples have been collected from these smokers but have not yet undergone laboratory testing and analysis. It is hoped that results from the follow-up study, when they become available, will provide Philip Morris USA and the public health community with information about whether and to what extent these smokers engaged in compensation.

12. To date, Philip Morris USA has spent approximately $30 million on the TES, Pilot Study, and follow-up study.

13. The TES collected an enormous volume of biological samples. For example, the amount of urine collected by the TES would be enough to fill close to 5,000 2-liter soda bottles.

14. The TES has produced an enormous amount of data. Altogether, there are approximately 3.8 million individual datapoints. It involves 20- to 100- times more statistical analyses than clinical trials run by pharmaceutical companies for new drug applications. These data, printed out, would be enough to fill two eighteen-wheeler trucks.

15. The TES is an ongoing research study. As described in further detail below, Philip Morris USA has barely begun processing and analyzing the immense volume of data generated by the TES. Philip Morris USA is not in a position to draw inferences based on these data, and the results of the TES are not yet known.

B. Plans, Status and Ongoing Nature of the TES

16. Philip Morris USA intends for the TES to conform to the highest scientific standards. To that end, a detailed Research Protocol was prepared to govern the execution of the TES, as well as a 203-page Statistical Analysis Plan for analyzing the data. The Statistical Analysis Plan took one full year to develop and was finalized in advance of any data analysis.

17. Biological samples (for example, urine and blood) and other information were collected from study participants at 39 different location across the U.S. Due to the enormous volume of samples, 3 different bioanalytical laboratories were engaged to analyze these samples.

18. MDS-Pharma ("MDS"), a highly-regarded contract research organization, was engaged to integrate source TES data from study sites and bioanalytical laboratories into a single integrated database. A comprehensive data integration plan was created to govern this process, which involved integrating data in different formats, such as datafiles, documents and spreadsheets.

19. The MDS database may contain identifying information about individual study participants. To protect the identities of these participants, and to maintain the objectivity of the data, Philip Morris USA does not have access to this database at this

time. The consent form signed by study participants restricts Philip Morris USA's access to identifying information, stating "The Sponsor, Philip Morris USA, will only see the study data and results without your name on it. No identifying information will be given or shown to the Sponsor in any written, electronic or other form."

20. The database is governed by the standard operating procedures of MDS, which are designed to comply with Good Clinical Practices Guidelines adopted by the FDA. This means, among other things, that changes made to the database after it has been "locked" must be documented.

21. The MDS database has now been "locked." That does not, however, mean that the database is free from discrepancies and errors. To the contrary, "locking" the database is only the beginning of the long process of evaluating plausibility of the data and correcting errors before statistical analysis of the data can begin. MDS is working with assistance from Philip Morris USA to detect and, where possible, correct, explain, or control for errors in the databases. Identifying, correcting, and accounting for these errors is standard scientific practice and is critical to producing results that will be accepted by other scientists as accurate and reliable.

22. The following are examples of some of the types of errors and implausibilities in the database that could lead to erroneous or misleading results unless corrected, explained, or otherwise taken into account:

- Participant X: Smoker, 1 cigarette smoked, high nicotine exposure

  Assume the database indicates that Study Participant X is a smoker, smoked 1 cigarette on the day of the study, and had a daily nicotine exposure of 10 mg. This level of nicotine exposure is many times what one would expect maximum daily nicotine exposure to be for a person who smoked only one cigarette. These data, therefore, are not plausible.

Transcription error is a possibility here. For example, it may be the case that Study Participant X smoked "10" cigarettes per day, not "1." Because study participants were required to submit to the study site the butts of all cigarettes smoked on the day of the study, it would be important to check the database for internal consistency to see whether Study Participant X submitted 1 cigarette butt or 10 cigarette butts. It would also be important to check the original survey form to determine how many cigarettes Study Participant X self-reports smoking per day. These survey forms are in the possession of the study sites. Philip Morris USA does not have access to these survey forms because they contain confidential identifying information about study participants. It would therefore be necessary to coordinate with the appropriate study site to ascertain how many cigarettes Study Participant X reported smoking per day in the original survey form.

- Participant Y: Non-Smoker, high nicotine exposure

Assume the database indicates that Study Participant Y is a non-smoker with a high daily nicotine exposure. This is not plausible, and several possible explanations should be investigated.

It may the case that Study Participant Y is a smoker, not a non-smoker. To investigate this possibility, one could examine TSNA exposure data for Study Participant Y, as measured by the biomarker NNAL.

If TSNA exposure is consistent with nicotine exposure, it suggests that Study Participant Y is in fact a smoker, because TSNAs are compounds that occur only in tobacco and tobacco smoke. This possibility could be further explored by consulting with the appropriate study site, which has access to the original survey forms containing confidential identifying information, to determine whether Study Participant Y self-reported as a smoker or a non-smoker.

TSNA exposure data may, on the other hand, confirm that Study Participant Y is a non-smoker. This suggests that the high daily nicotine exposure for Study Participant Y could be attributable to laboratory analytical error or the use of nicotine-containing products such as nicotine patches or nicotine gum. The latter in particular may be grounds to exclude these data from further analysis. The TES protocols specify that users of nicotine-containing products should be excluded from the study because such use may confound the results.

- Participant Z: Smoker, low nicotine and high carbon monoxide exposure

Assume the database indicates that Study Participant Z is a smoker with a low daily nicotine exposure and a high daily carbon monoxide exposure. This is questionable because daily nicotine and carbon monoxide exposure tend to correlate with one another (high with high, and low with low).

> The plausibility of these data could be investigated by consulting with the appropriate study site to determine the total volume of urine submitted by Study Participant Z. Nicotine exposure in the TES was measured by nicotine and nicotine biomarkers in urine. Study participants were required to collect all of the urine over the course of the day and submit it to the study site. A low volume of urine for Study Participant Z could suggest that this participant failed to comply with that important requirement, indicating that these data may need to be excluded in order to avoid erroneous results.

23. With approximately 3.8 million individual datapoints, the TES database is too immense to process and analyze all at once. Accordingly, a structured approach is being implemented in which specific subsets of data are processed and analyzed sequentially. The Statistical Analysis Plan is used to generate results from a specific data subset. These results take the form of computational or statistical analyses. In total, the TES will generate approximately 600 computational or statistical analyses, along with associated figures and charts.

24. After comprehensive evaluation of biological plausibility, the computational and statistical analyses for each data subset are to be incorporated into "Final Study Reports." There will be seven Final Study Reports. It is important to note that while the Final Study Reports compile computational or statistical results, they do not interpret these results or draw conclusions based upon them. The process of interpreting and drawing conclusions comes after the Final Study Report for a data subset is completed, in the course of preparing a manuscript for peer-review and publication in the scientific literature. After each Final Study Report is completed, the specific subset of the database that was used to produce that report will be cleaned of any confidential identifying information regarding study participants and then transferred by MDS to PM USA for use in preparing the manuscript. As this process moves forward, results for

individual biomarkers will be evaluated in the context of results for other biomarkers (when they become available) for coherence and plausibility.

25. The following chart indicates the order in which the TES data will be processed and the current estimated date of completion of the Final Study Reports.

Data Type	Processing and Analysis	Final Study Report (estimated)
COHb and Nicotine Equivalents	COHb and nicotine equivalents underway	4th quarter, 2005
Other Biomarkers of Exposure	not started	1st quarter, 2006
Biomarkers of Potential Harm	not started	3rd quarter, 2006
Model of Adult Smoking	not started	2nd quarter, 2007
Smoking Topography and others	not started	3rd quarter, 2007
Remaining Regressions	not started	1st quarter, 2008
Exploratory Analysis	not started	2nd quarter, 2008

As this chart indicates, processing and analysis of the carbon monoxide biomarker (COHb) and nicotine biomarkers is currently underway. The final statistical data sets for these biomarkers are not yet complete, and the Final Study Report is not expected until the last quarter of 2005.

26. We have established a very ambitious schedule for processing and analyzing data in a study of this scope and magnitude. I have instructed and believe that the processing and analysis of TES data is being completed as expeditiously as possible, consistent with the over-riding objective that the TES produce scientific results of the highest quality – whatever those results may be – that can stand up to rigorous peer-review and be published.

27. In designing and executing the TES, and in beginning to process and analyze its data, the scientists affiliated with the TES have developed experience,

understanding, and background knowledge that cannot be transferred or replicated based simply on reading documents. I believe that no one who is not currently affiliated with the TES would be able to process and analyze the TES data any faster than described as above, at least not if their purpose and intention is to produce results that are scientifically-rigorous and sound.

C. Plans to Publish and Disseminate Results of TES

28. Philip Morris USA has made the commitment that it will, once it submits a manuscript of results for a biomarker to a peer-reviewed journal, make the Final Study Report associated with that biomarker available to the scientific and public health communities upon request. This commitment has previously been communicated to the public health community, including to Dr. David Burns and Dr. Greg Connolly. Philip Morris USA plans to submit the first such manuscript in the third quarter of 2006. This manuscript will introduce the TES, address its design and methods, and discuss biomarker results for carbon monoxide and nicotine exposure.

D. Prior Published Exposure Studies

29. Cross-sectional studies that used biomarkers to measure smokers' exposure to smoke constituents have been conducted and published in the scientific literature for many years. At least twenty such studies are cited in Chapter 3 of NCI Monograph 13 (Tables 3-1 and 3-2), which was written by Dr. Neal Benowitz. Moreover, within the last month, Dr. Stephen Hecht has published a cross-sectional study of biomarkers for nicotine and lung carcinogens in smokers of cigarettes with varying FTC yields.

E. Consequences of Premature Disclosure of TES Data

30. It bears repeating that the TES was not conceived, designed, or executed for litigation. The protocols and processes that have been put into place for collecting, compiling, correcting, and analyzing TES data are intended to produce high quality scientific results that can be published by Philip Morris USA scientists and shared with the scientific and public health communities. Forced, premature disclosure of TES data would, for a number of reasons, substantially harm both the integrity of the TES and Philip Morris USA.

31. First, Philip Morris USA scientists have devoted years of their professional life to the TES, and they have a reasonable expectation that they – before anyone else – should be allowed to analyze the data and publish their results. That is general scientific practice, and depriving them of this opportunity would be fundamentally unfair.

32. Second, there is a substantial risk that analyses by an outside party based on TES data as they currently exist will be erroneous because the vast majority of the TES data exists in an unprocessed and uncorrected state. Philip Morris USA has established rigorous protocols to examine, correct, and quality-check data in the TES database, but that process has only just begun.

33. Third, erroneous results of an outside party that result from premature, forced production of TES data may – to the extent they become publicized, even if in the media – jeopardize the ability of Philip Morris USA scientists to publish the results of their analyses, even if those analyses are demonstrably based on the carefully-crafted protocols and processes described herein.

34. Finally, the premature, forced production of TES data will present Philip

Morris USA with a choice to either (a) continue the TES as planned and have no response to potentially erroneous analyses presented by Plaintiffs in litigation; or (b) derail its carefully-prepared scientific process and take shortcuts to develop its own rushed litigation response to the analyses offered by Plaintiffs in litigation. Neither of these choices are acceptable. Each choice would taint the TES with the adversial process, undermine its scientific integrity, and compromise the ability of Philip Morris USA scientists to publish their results. And neither of these choices is consistent with how good science should be done.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on 4/4/05.

Jane Y. Lewis, Ph.D.